Chemical Sciences Journal
ISSN: 2150-3494

Chaturvedi and Kamboj, Chem Sci J 2016, 7:2
DOI: 10.4172/2150-3494.1000e114

Editorial Open Access

Role of Schiff Base in Drug Discovery Research

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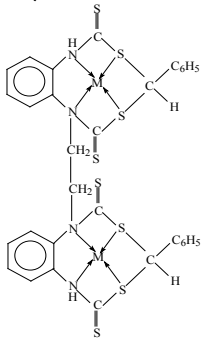
Compounds having imine or azomethine (–C=N–) functional group are known as Schiff bases. They were first reported in 1864 by German Chemist, Hugo Schiff and hence they are named so. For the synthesis of Schiff base, a number of methods have been described in literature. These are now synthesized by a simple one pot condensation of an various amines/hydrazides with carbonyl compounds, water is eliminated during condensation process. As shown in Figure 1, Schiff bases are synthesis from simple reaction between acetone and primary amine. Water is byproduct in this reaction.

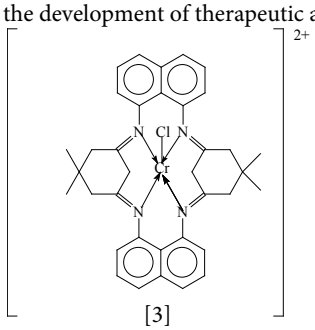
Other name for Schiff bases are imine or azomethine. Schiff bases form an backbone for large number of organic compounds and have a enormous applications in many fields. Structurally these are nitrogen derivatives of carbonyl compounds in which the (C=O) group has been replaced by an (C=N) group. Schiff bases have also received a great attention because of their potential biological activities such as anti-inflammatory, analgesic, antimicrobial, anticancer, antioxidant and so forth. Schiff Bases are the precursors of countless versatile organic processes for the production of intermediates/products and in making carbon-nitrogen linkage.

Synthesis, characterization and structure activity relationship (SAR) of Schiff bases are been studied worldwide. Several studies showed that the presence of a lone pair of electrons in sp^2 hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance [1]. They interferes in normal cell processes by the formation of a hydrogen bond between the active centers of cell constituents and sp^2 hybridized nitrogen atom of the azomethine group [2,3]. Schiff bases also have other potential applicability as catalysts, intermediates in organic synthesis, dyes, pigments, polymer stabilizers [4], and corrosion inhibitors [5]. Several Studies show that metal complexes of schiff base are more potent than free organic ligand [6]. Lots of researchers reported that addition of transition metals into Schiff bases increases its biological activity [7]. In coordination chemistry, Schiff bases has key role in design and development of novel compounds having potent biological activities. Schiff bases are the intermediates in organic reactions and are further explored for their utility. Schiff base and their derivatives has attracted the attention of researchers for exploring various processes for development of new environmental-friendly technology [8]. In medicinal field, due to chemotherapeutic applications Schiff bases is now attracting the attention of researchers. They are known to exhibit a variety of potent activities. Parveen and Arjmand [9] have reported the interaction of calf thymus (CT) DNA with a new asymmetric copper(II) N,N-ethane bridged N_2S_2 macrocycle [2].



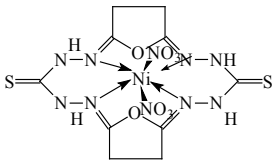
[2]

Rathi et al. prepared the trivalent transition metal tetraaza macrocyclic complexes from 1,8- diaminonaphthalene and 5,5-dimethylcyclohexane-1,3-dione [10]. They reported the antimicrobial and antioxidant activity of these complexes. They found that the Complex [3] shows the best antimicrobial as well as the best antioxidant activity. Therefore this compound can be promising lead for the development of therapeutic agent.

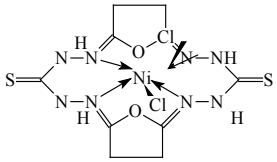


[3]

New octaazamacrocyclic complexes derived from furan-2,3-dione and thiocarbohydrazide was reported by Ref. [11]. The complex [4] shows the highest antimicrobial activity whereas the complex [5] was found to have good antioxidant agent.



[4]



[5]

Compound [6] and [7] are the antimicrobial drugs that consist of transition metal atoms in the macrocycle. Compund [6] was found to shows antibacterial activities against *E. coli* (-), *S. aureus* (+), *M. luteus* (+) and *B. licheniformis* (+) whereas [7] shows a very good antifungal activity towards *Aspergillus flavus* and *A. niger*.

In Figure 2, Azomethines constitute one of the most important class of nitrogen donor ligands in coordination chemistry. Metal complexes of Schiff bases are used in radiopharmaceuticals for cancer targeting [12]. The mechanism of working of such compounds may be on the basis of hydrogen bond formation by the azomethine group (-C=N-) at the active centers of cellular entities, which cause the interferences in normal cellular phenomenon. An interesting application of Schiff base is their use as catalysts. Schiff base complexes of Heterotrinuclear

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Received April 21, 2016; **Accepted** April 22, 2016; **Published** April 26, 2016

Citation: Chaturvedi D, Kamboj M (2016) Role of Schiff Base in Drug Discovery Research. Chem Sci J 7: e114. doi:10.4172/2150-3494.1000e114

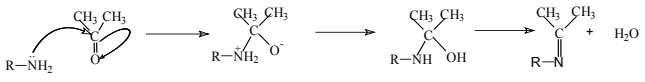
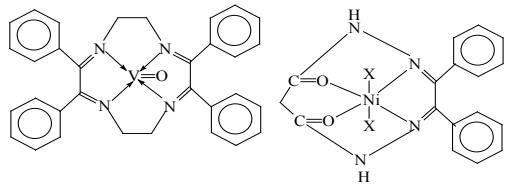


Figure 1: The condensation process in which water is eliminated.



[6] [7]

Where X=Cl

Figure 2: Antimicrobial drugs consist of transition metal atoms in the macrocycle.

manganese(II) and vanadium(IV) are used as catalysts for epoxidation of stryrene [13]. Schiff base complexes of cobalt are used as catalyst in redox carbonylation reaction [14]. This class of compounds has also exhibited activity against a wide range of organisms and is known to have medicinal importance and is used in drug design [15-17]. Antiparasitic activities of Azomethines derivatives have been reported by Rathelot et al. [18]. Azomethines have high potential chemical permutation and show diuretic [19], anticancer [20], antibacterial [21], antifungal and antioxidant activities [22].

The lipophilicity of the drug is increased through the formation of chelates and drug action is increased due to effective permeability of the drug into the site of action. The variation in the effectiveness of different compounds against different organisms depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells [23]. Because of the relative easiness of preparation, synthetic flexibility, and the special property of C=N group, Schiff bases are generally excellent chelating agents and have multidisciplinary applications. This class of compounds also exhibited remarkable activity against a wide range of organisms and are known to have medicinal importance and found applications in pharmacology and in drugs design.

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